Tracheal intubation in patients at risk for cervical spinal cord injury: A systematic review

Cabrini, Luca ; Baiardo Redaelli, Martina ; Filippini, Martina ; Fominskiy, Evgeny ; Pasin, Laura ; Pintaudi, Margherita ; Plumari, Valentina P ; Putzu, Alessandro ; Votta, Carmine D ; Pallanch, Ottavia ; Ball, Lorenzo ; Landoni, Giovanni ; Pelosi, Paolo ; Zangrillo, Alberto

Abstract: BACKGROUND Tracheal intubation in patients at risk for secondary spinal cord injury is potentially difficult and risky. OBJECTIVES To compare tracheal intubation techniques in adult patients at risk for secondary cervical spinal cord injury undergoing surgery. Primary outcome was first-attempt failure rate. Secondary outcomes were time to successful intubation and procedure complications. DESIGN Systematic review and meta-analysis of randomized controlled trials (RCTs) with trial sequential analysis (TSA). DATA SOURCES Databases searched up to July 2019. ELIGIBILITY Randomized controlled trials comparing different intubation techniques. RESULTS We included 18 trials enrolling 1972 patients. Four studies used the "awake" approach, but no study compared awake versus non-awake techniques. In remaining 14 RCTs, intubation was performed under general anesthesia. First-attempt failure rate was similar when comparing direct laryngoscopy or fiberoptic bronchoscopy versus other techniques. A better first-attempt failure rate was found with videolaryngoscopy and when pooling all the fiberoptic techniques together. All these results appeared not significant at TSA, suggesting inconclusive evidence. Intubating lighted stylet allowed faster intubation. Postoperative neurological complications were 0.34% (no significant difference among techniques). No life-threatening adverse event was reported; mild local complications were common (19.5%). The certainty of evidence was low to very low mainly due to high imprecision and indirectness. CONCLUSIONS Videolaryngoscopy and fiberoptic-assisted techniques might be associated with higher first-attempt failure rate over controls. However, low to very low certainty of evidence does not allow firm conclusions on the best tracheal intubation in patients at risk for cervical spinal cord injury.

DOI: https://doi.org/10.1111/aas.13532

DR LUCA CABRINI (Orcid ID : 0000-0001-8927-1197)

DR LORENZO BALL (Orcid ID : 0000-0002-3876-4730)

DR GIOVANNI LANDONI (Orcid ID : 0000-0002-8594-5980)

Article type : Review

Tracheal intubation in patients at risk for cervical spinal cord injury: a systematic review

Authors:

Luca Cabrini [1,2]

Martina Baiardo Redaelli [1]

Martina Filippini [1]

Evgeny Fominskiy [1]

Laura Pasin [3]

Margherita Pintaudi [1]

Valentina Paola Plumari [1]

Alessandro Putzu [4]

Carmine D. Votta [1]

Ottavia Pallanch [1]

Lorenzo Ball [5,6]

Giovanni Landoni [1,2]

Paolo Pelosi [5,6]

Alberto Zangrillo [1,2]

1. Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy

2. Università Vita-Salute San Raffaele, Milan, Italy

3. Department of Anesthesia and Intensive Care, Ospedale S. Antonio-ULSS 6, Padua, Italy

4. Division of Anesthesiology, Department of Anesthesiology, Pharmacology, Intensive Care and Emergency Medicine, Geneva University Hospitals, Geneva, Switzerland

5. Anesthesia and Intensive Care, San Martino Policlinico Hospital, IRCCS for Oncology and Neurosciences, Genoa, Italy

6. Department of Surgical Sciences and Integrated Diagnostics, University of Genoa, Genoa, Italy

Corresponding author:

Luca Cabrini, MD.

Department of Anaesthesia and Intensive Care,

IRCCS San Raffaele Scientific Institute, Via Olgettina 60, 20132 Milan, Italy.

Università Vita-Salute San Raffaele, Via Olgettina 58, 20132 Milan, Italy

e-mail: cabrini.luca@hsr.it

Running title: Tracheal intubation in spinal cord injury: a systematic review and meta-analysis

Word count: 3298 words

Conflicts of interest: none declared.

Abstract

Background: tracheal intubation in patients at risk for secondary spinal cord injury is potentially difficult and risky.

Objectives: to compare tracheal intubation techniques in adult patients at risk for secondary cervical spinal cord injury undergoing surgery. Primary outcome was first-attempt failure rate. Secondary outcomes were time to successful intubation and procedure complications.

Design: systematic review and meta-analysis of RCTs with trial sequential analysis (TSA).

Data sources: databases searched up to July 2019.

Eligibility: randomized controlled trials comparing different intubation techniques.

Results: we included 18 trials enrolling 1972 patients. Four studies used the "awake" approach, but no study compared awake versus non-awake techniques. In remaining 14 RCTs, intubation was performed under general anesthesia. First-attempt failure rate was similar when comparing direct laryngoscopy or fiberoptic bronchoscopy (FOB) versus other techniques. A better first-attempt failure rate was found with videolaryngoscopy and when pooling all the fiberoptic techniques together. All these results appeared not significant at TSA, suggesting inconclusive evidence. Intubating lighted stylet allowed faster intubation. Postoperative neurological complications were 0.34% (no significant difference among techniques). No life-threatening adverse event was reported; mild local complications were common (19.5%). The certainty of evidence was low to very low mainly due to high imprecision and indirectness.

Conclusions: videolaryngoscopy and fiberoptic-assisted techniques might be associated with higher first attempt failure rate over controls. However, low to very low certainty of evidence does not allow firm conclusions on the best tracheal intubation in patients at risk for cervical spinal cord injury.

Registration number: CRD42018116672

Editorial Comment:

In this systematic review, different modes of endotracheal intubation in patients at risk of cervical spine injury were compared. Information from 18 RCTs and close to 2000 patients suggests that videolaryngoscopy and fiberoptic-assisted techniques may be superior to conventional intubation, however the certainty of evidence was low/very low, and the findings should be interpreted with this in mind

Introduction

Tracheal intubation in the operating room in adult patients with known or suspected instability of the cervical spine is commonly considered at risk for secondary iatrogenic spinal cord injury. Instability of the cervical spine can be defined as a clinical condition in which motion or compression of cervical spinal tract can cause a vertebral displacement that jeopardize the spinal cord or the nerve roots[1,2]. Instability is often secondary to a trauma injuring the cervical bony or ligamentous elements; non-traumatic causes are also possible, like congenital syndromes or acquired diseases (above all rheumatoid arthritis and spondyloarthropathies)[2].

Traditionally, tracheal intubation in normal subjects includes full extension of the atlanto-occipital and atlanto-axial joints, flexion of the lower cervical spine tract and direct laryngoscopy[3]: any of these factors could injury to the spinal cord if instability is present. Studies performed in cadaver models of cervical spine and clinical studies showed that basic and advanced airways maneuvers can be dangerous[1,2].

Semirigid collars are commonly used to restrict motion in patients at risk for spinal cord injury: unfortunately, they markedly limit mouth opening to less than 3 cm and removal of their anterior portion can be required during tracheal intubation[1,3]. Manual in-line stabilization (MILS) is considered a better option during intubation, but it could not completely prevent cervical spine movement and result in limited laryngoscopic view and potentially in difficult intubation[1,2].

Beside direct laryngoscopy, several tracheal intubation techniques (videolaryngoscopy, lighted stylets, fiberoptic stylets, supraglottic devices and awake fiberoptic intubation) have been evaluated in real or simulated cervical spine instability[1-3]. We performed a systematic review and meta-analysis of published randomized controlled trials (RCTs) comparing two or more tracheal intubation techniques in operating room in adults at risk for secondary cervical spinal cord injury, to identify the best technique in terms of efficacy and safety.

Methods

Protocol

We followed the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines[4], registered the protocol in the PROSPERO database (CRD42018116672), and followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines[5] (Table S1)

Search Strategy

PubMed, BioMed Central, EMBASE and the Cochrane Central Register of Clinical Trials were searched electronically for pertinent studies from inception until July 5th, 2019 by 7 investigators (MBR, MF, LP, MP, VPP, CDV, OP). The terms *intubation, spine injury, cervical, randomized controlled trial, and controlled trials* were searched in combination or alone. The full search strategy is reported in the supplement (Methods S1). Reference lists of RCTs were reviewed to maximize the search for relevant articles, together with review articles and systematic reviews on the same topic.

Study Selection

References obtained from database and literature were first independently examined at title/abstract level by the same seven investigators (MBR, MF, LP, MP, VPP, CDV, OP), with disagreement resolved by consensus with supervision of two investigators (LC, LB) and, if potentially pertinent, full articles were retrieved.

The following inclusion criteria were used to select potentially relevant studies: a) RCTs comparing different techniques for performing tracheal intubation; b) studies performed in adult patients (>16 years old) at risk for cervical spine cord injury; c) studies published in peer-reviewed journals with no language restriction or time limit. Exclusion criteria were: a) RCTs not comparing two or more intubation techniques (for instance, trials comparing two sedative regimens during a single intubation technique were excluded); b) studies performed outside the operating room; c) studies based on simulation. Patients were considered at risk for cervical spine cord injury according to the definitions applied in individual studies. Three investigators (LG, PP, AZ) selected studies for the final analysis independently assessing compliance to selection criteria. Divergences were solved by consensus.

Primary outcome was first-attempt intubation failure rate; secondary outcomes were time to successful intubation and neurological and non-neurological procedure complications.

Data Abstraction, Synthesis and Study Characteristics

Data were independently extracted by two authors (LC, MBR) into standardized collection forms for the evidence and outcomes. Disagreements were resolved by discussion or involving a third reviewer when required. All variables for which data were sought are listed in Table 1. No assumption or simplification was made upon the missing data.

We contacted corresponding authors for further information on missing data on first-attempt intubation failure and neurological complications or on unclear items in risk of bias assessment. In case of missing e-mail, we tried to retrieve e-mail from other publications or from Google.

Quality assessment

Risk assessment using the Cochrane Collaboration risk of bias tool was performed by two independent investigators (AP, EF)[6]. Included RCTs were assessed for: (1) random-sequence generation; (2) allocation sequence concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) completeness of outcome data; (6) selective reporting; (7) other sources of bias (baseline imbalance, co-intervention, fixed blocked randomization in a unblinded trial, major study deviation, fraud). Each domain was assessed as low, unclear, or high risk of bias. Due to the nature of interventions, blinding of participants, personnel, and outcome assessors seemed difficult and therefore not considered crucial for trials' risk of bias judgement. The overall study judgement was: a) low risk of bias if all crucial domains were judged to be at low risk of bias; b) high risk of bias if at least one crucial domain was judged to be at high risk of bias; c) unclear risk of bias if at least one unclear crucial domain was present, without other high risk domain.

The certainty of the body of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework.[7,8]

Statistical Analyses

Continuous variables were analyzed with the inverse variance method and were expressed as mean differences (MD) with 95% CI. Dichotomous variables were analyzed with the Mantel-Haenszel method and expressed as risk ratios (RR) and 95% confidence intervals (CI). A 2-tailed P value <0.05 was set for statistical significance. Heterogeneity was assessed with the $\chi 2$ test and the I^2 test, with I^2 >50% being considered substantial, where the random-effects model was used for the analyses. We did not assess publication bias with funnel plots since there were less than 10 trials for each pooled analysis. Post-hoc subgroup analysis according to trial's risk of bias was performed. Subgroup differences were tested using Chi-square statistics. Meta-analyses were performed using the statistical software Review Manager

(RevMan, version 5.3; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark, 2014).

A post hoc fixed-effects trial sequential analysis (TSA) was performed with the intent to maintain an overall 5% risk of type I error and a 20% risk of type II error, at a power of 80%.[9,10,11] For first-attempt intubation failure rate and postoperative neurological complications, we assumed a relative risk reduction of 30%, judged to be clinically plausible and relevant, and we derived the control event proportion from the actual control dataset. For time to intubation, we judged to be clinically plausible and relevant a mean difference of 30 seconds with a variance of 15 seconds. The resulting required information size was diversity-adjusted. We used the TSA software (TSA Viewer [Computer program], Version 0.9.5.5 Beta, Copenhagen Trial Unit, Centre for Clnical Intervention Research, Rigshospitalet, Copenhagen, Denmark, 2016).

Deviations from the initial protocol mainly consisted in the inclusion of GRADE assessment, subgroup analysis according to risk of bias, and TSA; all details are reported in the supplement (Methods S2).

Results

Study characteristics

Database searches and references screening yielded 2155 articles. Among these, we identified and retrieved 18 randomized clinical trials for inclusion evaluating 1972 patients (Figure 1). Table 1 summarized the characteristics of the analyzed studies.

All RCTs were single-center and included only patients undergoing elective surgery. In 13 studies the cervical spine was unstable or not yet cleared, while in 3 studies the instability of the spine was considered as exclusion criteria. Cervical spine immobilization during intubation was reported in 13/18 studies (72%), and the most frequently reported technique was manual stabilization (7 RCTs).

Three trials were judged to be at low risk of bias,[12,13,29] 13 at unclear risk[14-22,24-26,28] and 2 at high-risk.[23,27,] Random sequence generation was assessed as low-risk of bias in 16 trials, allocation concealment in 9 trials, completeness of outcome data in 8 trials, selective outcome reporting in 4 trials, and other bias in 15 trials (Figure 2 and S1, Table S2).

We contacted all corresponding authors but one (the e-mail was impossible to retrieve); details on retrieved information are reported in the supplement (Results S1).

Intubation with difference devices

The average success rate at the first intubation attempt was 86.1% (1629 successful first attempt in 1892 patients in the 15 studies reporting this outcome, with success rates ranging from 100% to 56%). The GRADE quality of evidence for first-attempt intubation rate is reported in Table 2.

In four studies an "awake" approach was used for endotracheal intubation in both groups [14-16, 28] . Awake fiberoptic bronchoscopy (FOB) compared to other awake techniques (videolaryngoscope, lighted intubating stylet, optical stylet and intubating laryngeal mask) did not result in significant difference in intubation failure rate (RR 0.73, 95% CI 0.40 to 1.31; p=0.29; I^2*= 37%*; TSA-adjusted CI 0.06-8.13; low certainty evidence – Figure 3.1) and resulted in higher intubation length (MD 43.36, 95% CI 23.01 to 63.70 seconds; p<0.0001; I^2=70%; low certainty evidence - Figure 3.2).

No study compared awake versus non-awake endotracheal intubation techniques.

In the remaining 14 RCTs[12,13,17-27,29] , intubation was performed under general anesthesia after administration of sedative and neuromuscular blocking agents. Since the evaluated techniques were highly heterogeneous, we decided to perform two main meta-analytic comparisons focused on the

devices commonly available in the operating room: a) direct, traditional Macintosh laryngoscopy versus other techniques (3 RCTs; Fig. 2); b) videolaryngoscopy versus other techniques (5 RCTs; Fig. 3). No significant difference was found in terms of first-attempt failure rate with Macintosh laryngoscope versus controls, despite numerically higher failure with direct laryngoscopy (RR 3.05, 95% CI 0.97 to 9.60; p=0.06 I^2*= 0%*; TSA not performed due to too low information size; very low certainty evidence – Figure 4.1); on the contrary, videolaryngoscopy was associated with lower first-attempt failure (RR 0.53, 95% CI 0.32 to 0.90; p=0.02; I^2=36%*;* TSA-adjusted CI 0.06-4.51; low certainty evidence – Figure 5.1). Direct laryngoscopy and videolaryngoscopy were associated with no significantly shorter time to intubation with respect to controls (moderate and low certainty evidence– Figure 4.2 and Figure 5.2).

The techniques using a fiberoptic device significantly improved first-attempt failure rate when compared to techniques without any kind of fiberoptic assistance (RR 0.64, 95% CI 0.47 to 0.88, p=0.005; I^2 =13%; TSA-adjusted CI 0.40-1.04; low certainty evidence - Fig. S4.1). FOB (either awake or non-awake) showed no difference in first attempt failure rate compared to other techniques (RR 0.81, 95% CI 0.60 to 1.10, p=0.18; TSA-adjusted CI 0.51-1.30; low certainty evidence – Fig. S5.1) and a non significant higher time to intubation (MD 22.69, 95% CI -1.15 to 46.52 seconds; p= 0.06; I^2=99%; low certainty evidence – Fig. S5.2). The use of a lighted stylet versus other techniques was associated with similar first-attempt intubation failure rate (RR 1.56, 0.35 to 6.90, p=0.56; TSA inconclusive; very low certainty evidence) and quicker intubation (MD -32.95, 95% CI -61.99 to -3.92 seconds; p=0.03; I^2=70%; very low certainty evidence – Fig. S6.2). Optical stylet use showed no difference in failure rate (RR 0.96; 0.49 to 1.87, p=0.90; TSA-adjusted CI 0.06-14.68; very low certainty evidence) and time to intubation versus other techniques (Fig. S7). Complete analyses are available in the supplemental material.

Subgroup analyses according to risk of bias for the primary outcome did not suggested significant subgroup effect. Conflicting results have been found in lighted stylet trials, with a significant subgroup differences (p between groups=0.01); the difference in outcome estimate was mainly driven by one trial with opposing results than other trials (Results S2).

Two RCTs were not included in the aggregate analysis: one RCT with high risk of bias on the use of three different videolaryngoscopes with similar first-attempt intubation rate (>92%);[23] another RCT on two different intubation techniques via laryngeal mask airway that did not assess first-time intubation rate.[26]

Postoperative complications

Data on new postoperative neurological complications potentially associated to intubation where retrieved from 9 studies[13-15,21-23,25,28,29], with 7 trials with zero events in all groups and 2 trials with neurological complications. One study comparing intubation using a lighted intubating stylet (ILS) versus an intubating laryngeal mask reported 3 neurological complications (2 in the ILS group - no significant difference) detected one week after intubation at routine follow-up[21]. Unfortunately, no details were reported on the nature of the neurological complications, on the timing of their appearance and if they were or not transitory. The corresponding author of one trial reported a case of numbness in the right upper limb postoperatively in the ultrasound group, spontaneously resolved after 5 days[22] . Overall, the rate of postoperative neurological complications in the 9 studies with available data was 4/1177 (0.34%, including one immediately postoperatively[22] and three detected at one-week follow up[21]). The TSA was not performed due to too low information size.

No life-threatening adverse event was reported. On the contrary, non-neurologic local mild complications like epistaxis, transient change in voice, minor injury to the lip or tongue, or sore throat were common (tab. 1) (a total of 360 mild local complications in 1846 patients in 14 studies (19.5%).

Discussion

This is the first systematic review of randomized controlled trials comparing two or more techniques for endotracheal intubation in the operating room in adult patients at risk for cervical spinal cord injury. We identified 18 RCTs, comparing several different devices in heterogeneous combination. First-attempt intubation success rate and time to intubation differed among different techniques and among studies. Our results suggest that videolaryngoscope and more in general all the techniques using some kind of fiberoptic assistance might offer some benefit over controls in terms of first-attempt intubation rate. The incidence of postoperative neurological complication was low (0.36%) and the causality of the relationship with the intubation procedure remains uncertain, given that just one of them was noticed immediately after surgery[22] while others were detected at one-week follow-up[21] when a spontaneous spinal cord worsening or other intraoperative or postoperative events could have caused the neurological complications[1,2]. Non-neurological local complications were more common but no major adverse event was reported. Anyway, there is very low certainty of evidence supporting the safe use of a wide range of devices in this clinical setting and their use should be careful, regardless of the technique chosen.

Direct laryngoscopy in normal patients causes motion of the vertebral bodies, mostly at the craniocervical junction; in injured spine cadaver models, spine displacement resulted significantly more marked[1-3]. Neck

immobilization is effective in reducing spine motion, but markedly limits the visualization of the glottis during laryngoscopy[2,3] creating the conditions for a difficult intubation as very recently confirmed in the guidelines for intubation in the critically ill[20]. Furthermore, whatever the technique of neck immobilization adopted (including manual in-line stabilization, commonly considered the best choice) spine motion is still possible and potentially dangerous[1,3]. The impact in daily practice of these factors in patients at risk of secondary spinal cord injury during intubation has been evaluated in small observational studies: most Authors reported no new neurologic deficit after intubation, but case-reports of intubation-associated neurologic deterioration (sometime of devastating clinical severity) have also been published[1,2]. On the other hand, ascending myelopathy due to inflammatory and vascular reasons occurring up to 4 weeks after injury is sometimes present and makes it more difficult to ascertain the role of intubation[1,2].

Awake FOB is often considered the safest technique in patients at risk for spinal cord injury, but it requires time, experience, and a stable and cooperative patient[1,30,31]. Surveys conducted among anesthesiologists showed that most of them expressed a preference for awake FOB in case of unstable cervical spine, but almost half of them reported insufficient skill in the technique[32,33]. Available data are unable to confirm the superiority of awake FOB over other awake techniques in terms of success or safety in this setting, but its role in anticipated difficult airway is supported by several international guidelines[34-36]. Moreover, awake intubation can avoid basic airway maneuvers (particularly mask ventilation, potentially more dangerous of any intubation procedure[1]) and permits post-intubation neurological assessment and documentation, relevant in the peculiar class of patients considered. Unfortunately, so far no RCT has evaluated awake FOB (or any other awake technique) compared to tracheal intubation under general anesthesia.

Recently, a systematic review and meta-analysis of 24 RCTs comparing Macintosh laryngoscopy to alternative intubation techniques in patients with cervical spine immobilization reported that the Airtraq device might reduce the risk of intubation failure and the intubation time[37]. However, almost all the analyzed studies excluded patients really at risk for spinal cord injury, so their findings may be considered as only surrogates in terms of efficacy and of limited value in terms of safety. To avoid this limitations we included only studies evaluating patients at risk for neurological complications: we identified three studies evaluating direct laryngoscopy and aggregate data found similar intubation time and a numerically higher first-attempt intubation failure rate, not reaching statistical significance. Alternative techniques or devices to direct laryngoscopy include videolaryngoscopes, lighted or optical stylets, supraglottic devices and fiberoptic intubation. Their pros and cons in this setting are described elsewhere[2,3]; notably, the role of supraglottic devices is still controversial, as cervical vertebrae might be displaced posteriorly during

insertion[2,3]. Our analyses show that videolaryngoscopy and more in general all the techniques using fiberoptic assistance might offer higher success rates in this setting: no firm conclusions can be made at present, but their use could be taken into consideration by appropriately trained anesthesia providers. Moreover, videolaryngoscopes are continuously evolving and quite different in terms of angulation of the blade, presence or not of a channel for the tube, handling of the device and hence length of the learning curve [38-40]; ultimately, all these characteristics can impact their performances in different settings[40-43] . Generalizability of the results observed with one device to other videolaryngoscopes may be misleading.

We underline that the incidence of failure at the first attempt was relevant (mean 14%) and heterogeneous with different devices, so a plan B with a second choice device or technique should be in place and the operators should be adequately trained.

We found an incidence of neurological complications of 0.34%, immediately postoperatively in one case[14] and later in the other three[21], with undetermined correlation with intubation procedure. Criteria to identify if a new cord injury should be considered intubation-induced have been proposed, but never validated[44]. Available data are clearly insufficient to identify if one technique is safer than others.

Our review presents limitations: first, the identified RCTs were often small and evaluated heterogeneous techniques, so a limited number of quantitative analyses were possible. Nevertheless, we present the best available, most comprehensive and reliable picture on the topic, as we focused on studies including only patients really at risk of spinal cord injury. Second, data on safety must be interpreted cautiously in light of the limited information size. We must acknowledge that the low incidence and the missing data on neurological complications, despite the contact of corresponding authors, limit the relevance of the results. Third, all RCTs excluded emergent surgical patients: we have no data on the performance of the different intubating techniques in this setting. Finally, the overall information size and quality of evidence is low not supporting firm conclusions on the topic. Larger RCTs are required to better assess the benefits and risks of each technique, particularly when comparing awake versus non-awake techniques.

In conclusion, low certainty of evidence suggests the superiority of videolaryngoscopy and of intubation techniques using fiberoptic assistance over controls in terms of first attempt failure rate. However, low to very low certainty of evidence does not allow firm conclusions on the best intubation device in patients at risk for cervical spinal cord injury. The rate of neurological complications resulted rather low and probably unrelated to a specific intubation technique.

Acknowledgements

We thank Doctor Pierfrancesco De Domenico for the help in the revision process.

Financial support and sponsorship

Departmental funding only.

Conflicts of interest

The authors have no conflicts of interest.

Presentations of preliminary data

None declared.

Details of authors' contributions

MBR, MF, LP, MP, VPP, CDV, OP searched electronically for pertinent studies, supervised by LC and LB.

GL, PP and AZ selected studies for the final analysis independently assessing compliance to selection criteria.

LC and MBR independently extracted data into standardized collection forms and created tables for the evidence and outcomes.

AP and EF performed risk assessment as independent investigators.

References

1. Crosby ET. Airway management in adults after cervical spine trauma. Anesthesiology 2006;104:1293-318.
2. Martini RP, Larson DM. Clinical evaluation and airway management for adults with cervical spine instability. Anesthesiol Clin 2015;33:315-27.
3. Austin N, Krishnamoorthy V, Dagal A. Airway management in cervical spine injury. Int J Crit Illn Inj Sci 2014;4:50-6.
4. Shamseer L, Moher D, Clarke M et al. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015.349:g7647.
5. Liberati A, Altman DG, Tetzlaff J, et al.The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009 Jul 21;339:b2700. doi: 10.1136/bmj.b2700.
6. Higgins JPT, Green S (editors). Cochrane handbook for systematic reviews of interventions version 5.1.0 (updated March 2011). The Cochrane Col- laboration, 2011. www.handbook.cochrane.org.
7. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck- Ytter Y, Alonso-Coello P, Schünemann HJ; GRADE Working Group: GRADE: An emerging consensus on rating quality of evidence and strength of recommen- dations. BMJ 2008; 336:924–6.
8. Guyatt G, Oxman AD,Akl EA, Kunz R,Vist G, Brozek J, Norris S, Falck-Ytter Y, Glasziou P, DeBeer H, Jaeschke R,Rind D,Meerpohl J,Dahm P,Schünemann HJ: GRADE guidelines: 1. Introduction-GRADE evi-dence profiles and summary of findings tables. J Clin Epidemiol 2011; 64:383–94.
9. Brok J, Thorlund K, Wetterslev J, et al: Apparently conclusive meta- analyses may be inconclusive–trial sequential analysis adjustment of random error risk due to repetitive testing of accumulating data in apparently conclusive neonatal meta-analyses. Int J Epidemiol 2009; 38:287–298.
10. Thorlund K, Devereaux PJ, Wetterslev J, et al: Can trial sequential monitoring boundaries reduce spurious inferences from meta-analy- ses? Int J Epidemiol 2009; 38:276–286.
11. Thorlund K, Engstrøm J, Wetterslev J, et al: User manual for trial sequen- tial analysis (TSA). Copenhagen Trial Unit, Centre for Clinical Interven- tion Research, Copenhagen, Denmark. User Man

trial Seq Anal (TSA) Copenhagen Trial Unit, Cent Clin Interv Res Copenhagen, Denmark 2011:1–115. Available at: www.ctu.dk/tsa . Accessed May 15, 2018.

12. Kim E, Kim BG, Lim YJ, et al. A Comparison Between the Conventional and the Laryngoscope-Assisted Lightwand Intubation Techniques in Patients With Cervical Immobilization: A Prospective Randomized Study. Anesth Analg 2017;125:854-859.
13. Seo H, Kim E, Son JD, Ji S, Min SW, Park HP. A prospective randomised study of a rigid video-stylet vs. conventional lightwand intubation in cervical spine-immobilised patients. Anaesthesia 2016; 71:1341-1346.
14. Jadhav T, Sriganesh K, Reddy M, Chakrabarti D. Comparative study of fiberoptic guided versus intubating laryngeal mask airway assisted awake orotracheal intubation in patients with unstable cervical spine. Minerva Anestesiol 2017;83:804-811.
15. Mahrous RSS, Ahmed AMM. The Shikani Optical Stylet as an Alternative to Awake Fiberoptic Intubation in Patients at Risk of Secondary Cervical Spine Injury: A Randomized Controlled Trial. J Neurosurg Anesthesiol 2018;30:354-358.
16. Saha AK, Higgins M, Walker G, Badr A, Berman L. Comparison of awake endotracheal intubation in patients with cervical spine disease: the lighted intubating stylet versus the fiberoptic bronchoscope. Anesth Analg 1998;87:477-9.
17. Bharti N, Arora S, Panda NB. A comparison of McCoy, TruView, and Macintosh laryngoscopes for tracheal intubation in patients with immobilized cervical spine. Saudi J Anaesth 2014;8:188-92.
18. Chalam KS, Gupta J. Comparison of intubating laryngeal mask airway and fiberoptic bronchoscopy for endotracheal intubation in patients undergoing cervical discectomy. J Anaesthesiol Clin Pharmacol 2016;32:515-518.
19. Fan H, Cao H, Sun Y, et al. Endotracheal intubation in elective cervical surgery: A randomized, controlled, assessor-blinded study. Medicine 2017;96:e7817.
20. Gupta N, Rath GP, Prabhakar H. Clinical evaluation of C-MAC videolaryngoscope with or without use of stylet for endotracheal intubation in patients with cervical spine immobilization. J Anesth 2013;27:663-70.
21. Inoue Y, Koga K, Shigematsu A. A comparison of two tracheal intubation techniques with Trachlight and Fastrach in patients with cervical spine disorders. Anesth Analg 2002;94:667-71.

22. Moustafa MA, Arida EA, Zanaty OM, El-Tamboly SF. Endotracheal intubation: ultrasound-guided versus fiberscope in patients with cervical spine immobilization. J Anesth 2017;31:846-851.

23. Shravanalakshmi D, Bidkar PU, Narmadalakshmi K, Lata S, Mishra SK, Adinarayanan S. Comparison of intubation success and glottic visualization using King Vision and C-MAC videolaryngoscopes in patients with cervical spine injuries with cervical immobilization: A randomized clinical trial. Surg Neurol Int 2017;8:19.

24. Xu M, Li XX, Guo XY, Wang J. Shikani Optical Stylet versus Macintosh Laryngoscope for Intubation in Patients Undergoing Surgery for Cervical Spondylosis: A Randomized Controlled Trial. Chin Med J 2017;130:297-302.

25. Yumul R, Elvir-Lazo OL, White PF, et al. Comparison of the C-MAC video laryngoscope to a flexible fiberoptic scope for intubation with cervical spine immobilization. J Clin Anesth 2016:46-52.

26. Malcharek MJ, Rockmann K, Zumpe R, et al. Comparison of Aintree and Fastrach techniques for low-skill fibreoptic intubation in patients at risk of secondary cervical injury: a randomised controlled trial. Eur J Anaesthesiol 2014;31:153-8.

27. Wu CN, Ma WH, Wei JQ, et al. Laryngoscope and a new tracheal tube assist lightwand intubation in difficult airways due to unstable cervical spine. PLoS One 2015;10:e0120231.

28. Dutta K, Sriganesh K, Chakrabarti D, Pruthi N, Reddy M. Cervical Spine Movement During Awake Orotracheal Intubation With Fiberoptic Scope and McGrath Videolaryngoscope in Patients Undergoing Surgery for Cervical Spine Instability: A Randomized Control Trial. J Neurosurg Anesthesiol. 2019 Mar 28. doi: 10.1097/ANA.0000000000000595. [Epub ahead of print]

29. Ozkan D, Altinsoy S, Sayn M, et al. Comparison of cervical spine motion during intubation with a C-MAC D-Blade and a LMA Fastrach. Anesthesist. 2019; 68(2):90-96

30. Higgs A, McGrath BA, Goddard C, et al; Difficult Airway Society; Intensive Care Society; Faculty of Intensive Care Medicine; Royal College of Anaesthetists. Guidelines for the management of tracheal intubation in critically ill adults. Br J Anaesth 2018;120:323-352

31. Cabrini L, Baiardo Redaelli M, Ball L, et al. Awake Fiberoptic Intubation Protocols in the Operating Room for Anticipated Difficult Airway: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Anesth Analg 2019;128:971-980.

32. Jenkins K, Wong DT, Correa R. Management choices for the difficult airway by anesthesiologists in Canada. Can J Anaesth 2002;49:850-6.

33. Ezri T, Szmuk P, Warters RD, Katz J, Hagberg CA. Difficult airway management practice patterns among anesthesiologists practicing in the United States: have we made any progress? J Clin Anesth 2003;15:418-22.

34. Apfelbaum JL, Hagberg CA, Caplan RA, et al; American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Anesthesiology 2013;118:251-70.

35. Petrini F, Accorsi A, Adrario E, et al.; Gruppo di Studio SIAARTI "Vie Aeree Difficili"; IRC e SARNePI; Task Force. Recommendations for airway control and difficult airway management. Minerva Anestesiol 2005;71:617-57.

36. Law JA, Broemling N, Cooper RM, et al; Canadian Airway Focus Group. The difficult airway with recommendations for management--part 2--the anticipated difficult airway. Can J Anaesth 2013;60:1119-38.

37. Suppan L, Tramèr MR, Niquille M, Grosgurin O, Marti C. Alternative intubation techniques vs Macintosh laryngoscopy in patients with cervical spine immobilization: systematic review and meta-analysis of randomized controlled trials. Br J Anaesth 2016;116:27-36.

38. Butchart AG, Young P. The learning curve for videolaryngoscopy. Anaesthesia. 2010;65:1145-6

39. Cavus E, Byhahn C, Dörges V. Classification of videolaryngoscopes is crucial. Br J Anaesth 2017;118:806-807.

40. Kleine-Brueggeney M,Greif R, Schoettker P, Savoldelli GL, Nabecker S, Theiler LG. Evaluation of six videolaryngoscopes in 720 patients with a simulated difficult airway: a multicentre randomized controlled trial. Br J Anaesth 2016;116:670-9.

41. Lewis SR, Butler AR, Parker J, Cook TM, Schofield-Robinson OJ, Smith AF. Videolaryngoscopy versus direct laryngoscopy for adult patients requiring tracheal intubation: a Cochrane Systematic Review. Br J Anaesth 2017;119:369-383.

42. Pieters BMA, Maas EHA, Knape JTA, van Zundert AAJ. Videolaryngoscopy vs. direct laryngoscopy use by experienced anaesthetists in patients with known difficult airways: a systematic review and meta-analysis. Anaesthesia 2017;72:1532-1541.

43. Jaber S, De Jong A, Pelosi P, Cabrini L, Reignier J, Lascarrou JB. Videolaryngoscopy in critically ill patients. Crit Care 2019;23:221

44. McLeod AD, Calder I. Spinal cord injury and direct laryngoscopy--the legend lives on. Br J Anaesth 2000;84:705-9.

FIGURE CAPTIONS:

Figure 1 - PRISMA flow diagram.

Figure 2 - Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

Figure 3 - Meta-analysis of awake techniques: fiberoptic bronchoscopy vs control (1.First-attempt intubation failure; 2.Time to intubation).

Figure 4 - Meta-analysis of Macintosh laryngoscopy vs control (1.First-attempt intubation failure; 2.Time to intubation).

Figure 5 - Meta-analysis of videolaryngoscopy vs control (1.First-attempt intubation failure; 2.Time to intubation).

Table 1 - Characteristics of the included studies

First author	Patients' characteristics	N	Techniques				First attempt success (%)				Time to intubation (mean±SD,sec)				NON neurologic complications,n (%)			
			Intervention	Control			Intervention	Control			Intervention	Control			Intervention	Control		
				1st	2nd	3rd		1st	2nd	3rd		1st	2nd	3rd		1st	2nd	3rd
Bharti N[17]	ASA 1-2 with cervical trauma undergoing cervical spinal surgery	40	Traditional (Macintosh) laryngoscope	McCoy laryngoscope	TruView EVO2	/	84%	91%	95%	/	30 ± 11	34 ± 8	36 ± 7	/	3 17,7%	7 39%	/	/
Chalam KS[18]	ASA 1-2 undergoing elective cervical disc surgery	60	Intubating laryngeal mask (ILMA)	FOB	/	/	90%	90%	/	/	38 ± 11	30 ± 14	/	/	4 13%	3 10%	/	/
Dutta K[28]	ASA1-2 with upper cervical spine(C1-C4) instability undergoing elective stabilization surgery	46	McGrath videolaryngoscope	FOB	/	/	78%	78%	/	/	67±37	86±45	/	/	na	na	/	/
Fan H[19]	ASA 1-2 with cervical spine disease undergoing anterior cervical spine surgery	30	GlideScope video laryngoscope	Ctrachlaryngealmaskairway	Shikani optical stylet	/	100%	87%	87%	/	18 ± 3	80 ± 22	40 ± 14	/	0	4 26,7 %	4 26,7 %	/
Gupta N[20]	ASA1-2 undergoing cervical spine surgery for cervical compressive mielopathy	120	traditional (Macintosh) laryngoscope with non-styletted ETT	Traditional Macintosh laryngoscope with styletted ETT	C-MAC with non-styletted ETT	C-MAC with styletted ETT	90%	93%	100 %	100 %	34 ± 37	34 ± 24	52±37	27±6	6 20%	3 10%	3 10%	2 6.6 %
Inoue Y[21]	ASA 1,2 scheduled to undergo cervical spine surgery	148	LightedIntubatingStylet (Trachlight)	Intubatingl aryngealmask (Fastrach)	/	/	90%	57%	/	/	23 ± 9	71 ± 24	/	/	2 3%	14 19%	/	/

Jadhav T[14]	ASA 1-3 scheduled for elective stabilization surgery	32	FOB	intubatingl aryngealma sk (ILMA)	/	/	56%	69%	/	/	na	na	/	/	1 6%	4 25%	/	/
Kim E[12]	Patients of ASA grade I-II requiring cervical spine immobilization for cervical spine surgery	162	LightedIntubati ngStylet	Laryngosco pe-assisted Lighted Intubating Stylet	/	/	75%	89%	/	/	22± 13	24 ± 12	/	/	65 85%	35 42.7 %	/	/
Mahrous RSS[15]	ASA 1-3 having cervical instability or at risk of secondary cervical injury, scheduled for neurosurgical intervention.	60	Shikaniopticalst ylet	FOB	/	/	90%	100 %	/	/	53 ± 7	102 ± 11	/	/	4 13%	0	/	/
Malcharek MJ[26]	ASA 1-3 scheduled for neurosurgery of the cervical spine	80	Aintree IntubationCath eter via cLMA + FOB	Fastrach + FOB	/	/	/	/	/	/	260± 91	289± 107	/	/	na	na	na	/
Moustafa MA[22]	ASA 1,2 with suspected cervical spine instability	266	Ultrasoundguid edintubation	FOB	/	/	72%	80%	/	/	57 ± 12	55 ± 10	/	/	22 16,6%	12 9%	/	/
Özkan D[29]	ASA 1-3 undergoing elective cervical discectomy	52	C-MAC D-blade	Fastrach	/	/	100%	77%	/	/	na	na	/	/	0	0	/	/
Saha AK[16]	ASA 1-3 scheduled for cervical stabilization (myelopathy or radiculopathy)	38	LightedIntubati ngStylet	FOB	/	/	65%	89%	/	/	19 ± 15	81 ± 63	/	/	1 5%	7 39%	/	/

Seo H[13]	ASA 1,2 scheduled for cervical spine surgery	168	Optiscoperigid video-stylet	Surch-Lite Lighted Intubating Stylet	/	/	90%	87%	/	/	19 (12-41) IQR	15 (8-29)	/	/	22 26,2%	33 39.3 %	/	/
Shravanalakshmi D[23]	ASA 1,2 with proven or sospected cervical spine injury	135	King Vision videolaryngoscope	C-MAC C-blade	C-MAC D-blade	/	93%	100 %	96%	/	25 ± 7	23 ± 5	27 ± 7	/	1 2.2%	0	0	/
Wu CN[27]	ASA 1-3 with unstable cervical disease	90	Lighted Intubating Stylet with traditional laryngoscopy but using WEI Jet ETT	LightedIntubatingStylet alone	Laryngoscope - assisted Lighted Intubating Stylet	/	100%	63%	83%	/	111 ± 18	63 ± 27	67 ± 29	/	/	/	/	/
Xu M[24]	ASA 1-3 with cervical spondylosis undergoing surgery	270	Shikani Optical Stylet	traditional (Macintosh) laryngoscope	/	/	99%	98%	/	/	25 ± 6	24 ± 6	/	/	27 20%	44 32.6 %	/	/
Yumul R[25]	ASA 1-3 undergoing elective cervical spine surgery	140	C-MAC video laryngoscope	FOB	/	/	83%	78%	/	/	35 ± 22	59 ± 36	/	/	22 31,4%	15 21,4 %	/	/

Abbreviations: N=number of analyzed patients; FOB= fiberoptic bronchoscopy; ETT= endotracheal tube; na=not available, SD= standard deviation

Devices description: Macintosh= conventional laryngoscope allowing direct vision; McCoy Laryngoscope (Penlon, UK)= a laryngoscope with a hinged tip allowing epiglottis elevation; TruView EVO2 (Truphatek International Ltd, Israel): a modified laryngoscope that expand the angular view of the larynx thanks to an optical system of prisms and lenses; ILMA (Teleflex Medical Europe Ltd, Ireland): laryngeal mask allowing blind intubation; Glidescope (Vearathon Inc, WA): a videolaryngoscope; CTrach laryngeal mask (The Laryngeal Mask Company, Singapore): a laryngeal mask that contains an integrated fiber-optic unit for the imaging of the glottis; Shikani optical stylet (Clarus Medical LLC, MN): an optical stylet with fiber-optic endoscopic imaging; C-MAC (Karl Storz, Germany): Mac Intosh shaped blade (C-Blade) or more angulated (D-Blade) videolaryngoscope; Trachlight (Laerdal Medical, NY): a lightwand intubating stylet; Fastrach (Intavent Ltd, UK): a laryngeal mask allowing intubation; Aintree intubating catheter (Cook Medical, USA): a blunt tip radipoaque catheter with centimeters mark; Optiscope (Clarus Medical, MN): a rigid video stylet providing direct images of airway structures; Surch-Lite (Bovie Medical, NY): a lightwand; King Vision (King Systems, IN): a videolaryngoscope.

Table 2 – First-attempt intubation failure rate - GRADE summary of findings.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with [comparison]	**Risk with [intervention]**			
Awake fiberoptic bronchoscopy vs. other awake techniques	225 per 1 000	**164 per 1 000** (90 to 294)	**RR 0.73** (0.40 to 1.31)	176 (4 RCTs)	⨁◯◯◯ VERY LOW
Macintosh laryngoscope vs. other techniques	17 per 1 000	**52 per 1 000** (16 to 163)	**RR 3.05** (0.97 to 9.60)	450 (3 RCTs)	⨁◯◯◯ VERY LOW
Fiberoptic devices vs. other techniques	156 per 1 000	**100 per 1 000** (73 to 137)	**RR 0.64** (0.47 to 0.88)	1052 (9 RCTs)	⨁⨁◯◯ LOW
Videolaryngoscopy vs. other techniques	167 per 1 000	**89 per 1 000** (54 to 151)	**RR 0.53** (0.32 to 0.90)	403 (5 RCTs)	⨁⨁◯◯ LOW
Fiberoptic bronchoscopy vs. other techniques	324 per 1 000	**263 per 1 000** (195 to 357)	**RR 0.81** (0.60 to 1.10)	542 (7 RCTs)	⨁⨁◯◯ LOW
Lighted stylet vs. other techniques	205 per 1 000	**320 per 1 000** (72 to 1 000)	**RR 1.56** (0.35 to 6.90)	438 (4 RCTs)	⨁◯◯◯ VERY LOW
Optical stylet vs. other techniques	62 per 1 000	**59 per 1 000** (30 to 116)	**RR 0.96** (0.49 to 1.87)	523 (4 RCTs)	⨁◯◯◯ VERY LOW

CI: Confidence interval; **RR:** Risk ratio

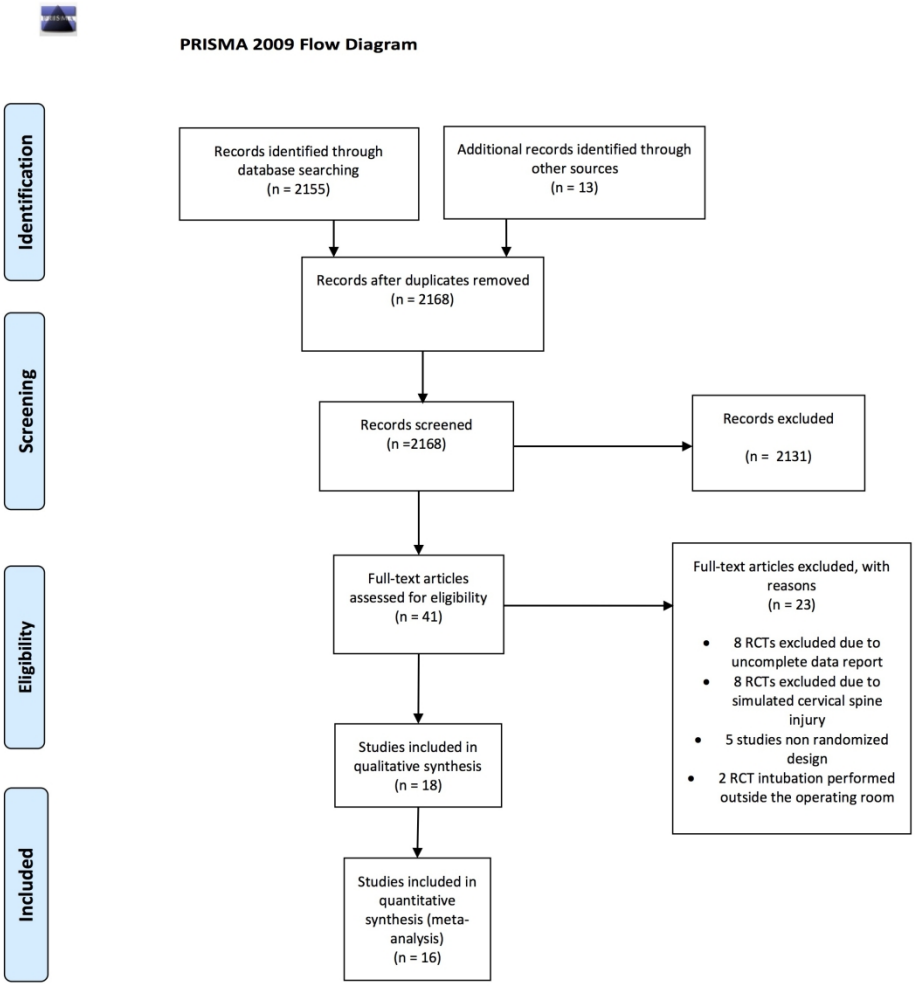
GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

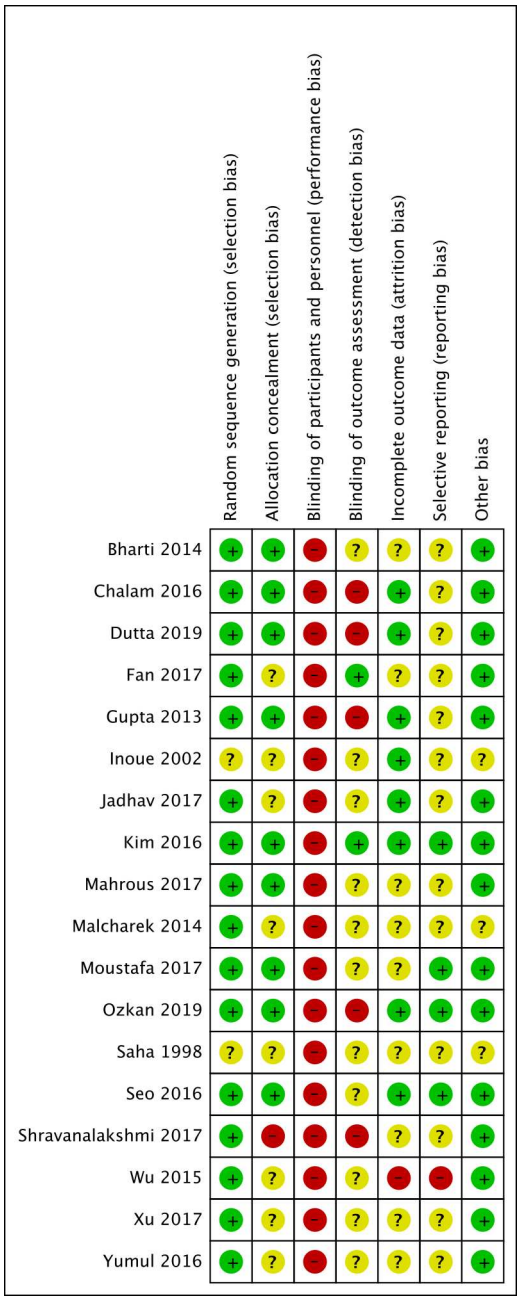
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect



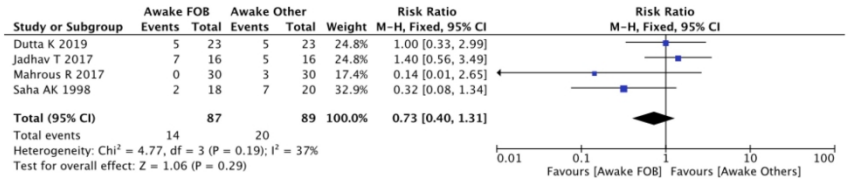
aas_13532_f1.jpg



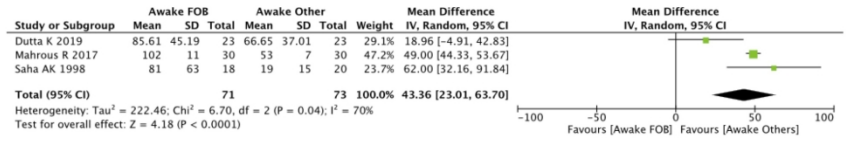
aas_13532_f2.tiff

Figure 3

1.



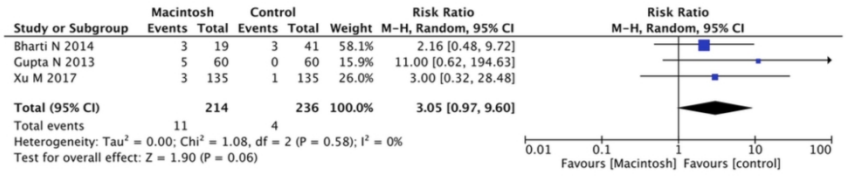
2.



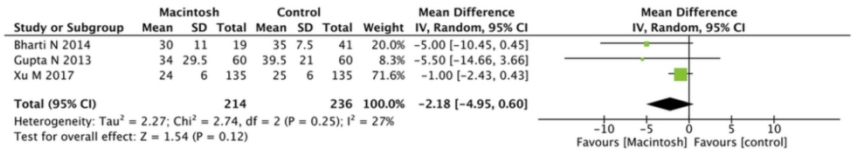
aas_13532_f3.jpg

Figure 4

1.



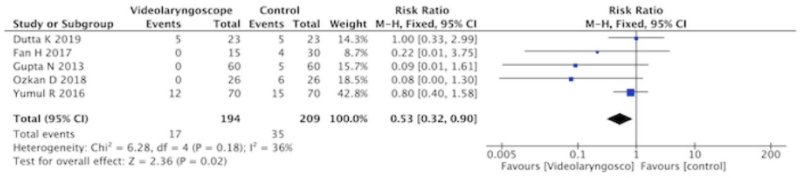
2.



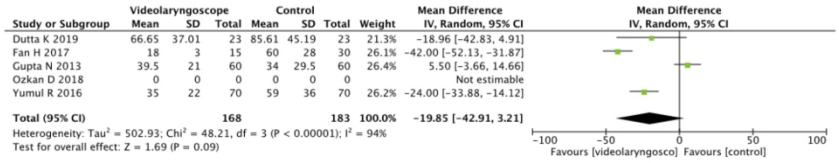
aas_13532_f4.jpg

Figure 5

1.



2.



aas_13532_f5.jpg